ECHOCARDIOGRAPHIC ASSESSMENT OF SYSTOLIC TIME INTERVALS IN HEMODIALYSIS PATIENTS WITH NORMAL EJECTION FRACTION

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CERTIFICATE

This is to certify that this dissertation entitled "**ECHOCARDIOGRAPHIC ASSESSMENT OF SYSTOLIC TIME INTERVALS IN HEMODIALYSIS PATIENTS WITH NORMAL EJECTION FRACTION**" Submitted by **DR.T.BALASUBRAMANIYAN**, appearing for D.M. Nephrology Degree Examination in February 2006 is a bonafide record of work done by him under my direct audience and supervision in partial fulfillment of regulation of the Tamilnadu Dr.M.G.R. Medical University, Chennai, I forward this to the Tamilnadu Dr.M.G.R. Medical University, Chennai, Tamilnadu, India.

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CONTENTS

INTRODUCTION

Chronic Kidney Disease (CKD) and Cardiovascular Disease (CVD) have been inextricably linked since the earliest days of chronic dialysis. Several statistics accrued since that time attest to the impact of cardiovascular disease in renal patients. Approximately one half of all deaths in end stage renal disease patients are attributable to cardiovascular disease, a proportion that is remarkably similar throughout the world. Several factors are thought to contribute to this high burden of cardiac disease in chronic kidney disease patients. First, the prevalence of many traditional risk factors for Cardiovascular disease such as diabetes, hypertension is higher among CKD patients than in general population. Second, several metabolic and hemodynamic disturbances that occur and progress in relation to declining renal function may modify cardiovascular risk. There is growing evidence that, uremia-related risk factors (Anemia, hypercholesterolemia, hyperhomocystinemia, divalent ion abnormalities, oxidative stress) contribute to the excess burden of cardiovascular disease in chronic kidney disease patients. The frequency of fatal and non-fatal

cardiovascular events is increased even in the earliest stages of chronic kidney disease[1]. It appears that uremia acts to amplify the incidence of fatal ischemic heart disease by a constant factor irrespective of the baseline incidence in the general population[2].

When maintenance hemodialysis was introduced by Scribner in 1960s, the naïve view prevailed that if one removed uremic toxins sufficiently well by dialysis life expectancy would approach that in the general population. This view was shattered by a report of Lindner et al documenting a strikingly increased rate of death from cardiovascular events in hemodialysis patients. Clyde shields, the first patient on longterm hemodialysis died of myocardial infarction in 1970 aged 50 years, eleven years after starting hemodialysis. The burden of cardiac disease in all phases of chronic kidney disease is high, and its clinical impact grave. The most frequent clinical manifestations are ischemic heart disease and congestive heart failure. Ischemic heart disease may be atherosclerotic or non atherosclerotic in origin. Congestive heart failure results from ischemic heart disease, cardiomyopathy or both. The manifestations of uremic cardiomyopathy include concentric left ventricular hypertrophy, eccentric left ventricular hypertrophy, Systolic

dysfunction and diastolic dysfunction. Risk factors for cardiac disease in uremia include age, diabetes-mellitus, hypertension, anemia, volume overload, hyperparathyroidism, dyslipidemia and perhaps uremia itself.

Although studies have traditionally focused on the dialysis population it has become evident that risk factors for cardiovascular disease and their initial consequences to the heart already are present during the predialysis phase and persist despite significant amelioration in the transplantation phase. Even so, our knowledge of these risks and consequences remains far from definitive, particularly in the chronic renal insufficiency and transplantation phases. Although much data exist on the impact of risk factor modification and therapy of congestive heart failure for the general population, corresponding trials in the renal population have not been done. It is useful to remember that many of the risks for cardiovascular diseases are common to both renal and non-renal population and the absolute benefit of any intervention tends to increase with increasing age.

In dialysis patients cardiovascular events are the most common cause of death[3-4]. A problem which had to some extent

been neglected in the past was cardiac failure as a cause of death. Cohort studies indicate that cardiac failure is a common and frequently lethal occurrence. Uremic cardiomyopathy presents as left ventricular hypertrophy, dilatation and coronary artery disease causing diastolic and systolic dysfunction[5-6]. Doppler derived systolic time intervals (STI) are useful indices of myocardial electromechanical systolic function[7-9].

The annual incidence of myocardial infarction or angina requiring hospitalization among hemodialysis patients is 8% and that of heart failure requiring hospitalisation or treatment with ultrafiltration is 10%[10]. Systolic dysfunction disorders that are predictive of congestive heart failure can be detectable even before the overt decline in left ventricular ejection fraction from the Doppler derived STI indices. Appropriate medical treatment or adequate ultrafiltration of patients at high risk (Prolonged STI index) for developing congestive heart failure, will decrease the death rate resulting from congestive heart failure.

OBJECTIVES

The objectives of this controlled study are:

i) Evaluate latent systolic dysfunction and

ii) Its relation with diastolic dysfunction in hemodialysis patients with normal ejection fraction, using Doppler derived systolic time intervals.

MATERIALS AND METHODS

Study Population:

The study population included 25 hemodialysis patients (21 male, 4 female, mean age 36± years) and 25 healthy controls (15male, 10 female, mean age 37± 10 years). Patients who were on dialysis longer than three months were included in this study. Eighteen patients were dialysed thrice weekly and the remaining seven patients received dialysis twice weekly. Patients with systolic and diastolic blood pressures above 140 and 90mm Hg were grouped as hypertensive. According to this classification, 44% of patients were hypertensive. The control group comprised of healthy normotensive persons with no cardiovascular complaints, normal electrocardiogram (ECG) and normal blood chemistries. The demographic features and biochemical parameters are shown in Table 1 and 2.

TABLE-1 Demographic features

No. of patients	25
Age (in years)	36±13
Sex - Male Female	21 4
Time spent on dialysis (months)	20±6
Dialysis frequency - Twice/Week Thrice/Week	07 (28%) 18 (72%)

Table -2 Biochemical parameters and basic renal disease

Predialytic blood Urea (mg/dl)	124±33
Predialytic creatinine (mg/dl)	7.9±1.3
Urea reduction ratio (URR%)	63.2±6.18
Haemoglobin (g/dl)	8.7±0.75
Serum Albumin (g/dl)	3.5±.74
Primary disease Chronic glomerulo nephritis Chronic interstitial nephritis Others	 14 (56%) 9 (36%) 2 (8%)

INCLUSION AND EXCLUSION CRITERIA

Hemodialysis patients who were on dialysis longer than three months were included in the present study (mean time on dialysis 20± 6months)

Patients with
- Diabetes mellitus
- Acute ischemic syndromes or
- Previous myocardial infarction
- Cardiac arrhythmias
- Valvular heart diseases
- Patients using Angiotensin converting enzyme inhibitors were excluded.

ECHOCARDIOGRAPHIC ANALYSIS

An echocardiographic examination was carried out by using a VINGMED CFM 725 echocardiographic system and a 2.5 MHZ phase- array transducer. Cardiac rhythm was recorded during the examination. Hemodialysis patients were examined using Doppler echocardiography the day after hemodialysis. The means of three consecutive measurements of the Doppler echocardiographic parameters on a good quality recording was taken for each parameter.

Because echocardiography is widely available, simple and reproducible it has become the method of choice for assessment of left ventricular hypertrophy. Epidemiology studies in non-renal population have established that the upper limits of left ventricular mass index are 130 grams per m^2 for adult men and 102 grams per m^2 for adult women. Values above these limits indicate left ventricular hypertrophy. The patterns of left ventricular hypertrophy on echocardiography are concentric hypertrophy, Eccentric hypertrophy or asymmetric septal hypertrophy. Concentric left ventricular hypertrophy is characterised by a

thickened left ventricular wall (>45%) more than 1.2cm during diastole with normal ventricular cavity volume. Eccentric left ventricular hypertrophy is characterised by increased left ventricular mass with increased ventricular cavity volume but the relative wall thickness may be normal or low (<45%). The calculation of left ventricular mass and volume , not independent of patient's volume status, hence the patient should be as close as possible to dry weight. In patients on hemodialysis, it is important to standardize the time and conditions of the study in relation to the dialysis session. Hence in end stage renal disease patients echocardiograms should be obtained the day after the dialysis session, with the patient at dry weight or at most, one kilogram above dry weight.

The criterion for left ventricular hypertrophy was left ventricular mass index of >134g/m^2 for men or > 110g/m^2 for women[11]. The left ventricular mass index was calculated by dividing the left ventricular mass with body surface area calculated from Dubois formula. Pulsed- Doppler flow samples from the mitral valve were taken during quiet breathing from a sample volume of

0.5cm that was placed at the tip of the mitral valve leaflets in the apical four chamber view[12].

Measured parameters were mitral early filling (E wave) Peak velocity (PV), mitral late filling (A wave) peak velocity, ratio of E wave PV to A wave PV, mitral deceleration slope and deceleration time. The isovolumetric relaxation time (IVRT) and isovolumetric contraction time were measured (IVCT). The interval from the end of aortic flow or aortic valve closure to the beginning of mitral flow or mitral valve opening was taken as the isvovolumetric relaxation time. The interval from the end of mitral valve closure to the beginning of aortic flow or aortic valve opening was taken as the isovolumetric contraction time (IVCT). The presence of abnormal left ventricular filling, distensibility and diastolic stiffness or in other words diastolic dysfunction was diagnosed according to the criteria of working group[13]. According to this criteria diastolic dysfunction is diagnosed when

Isovolumetric relaxation time > 100 m sec or

The E/A ratio <1.0 and

Deceleration time > 220 m sec

Systolic dysfunction is defined as an ejection fraction of less than 40% indicating impaired myocardial contractility. It often is associated with left ventricular dilatation (left ventricular end diastolic diameter >5.6cm) defined echocardiographically as left ventricular cavity volume index greater than 90ml per m^2.

The left ventricular systolic time intervals were measured by a simultaneous recording of cardiac rhythm and aortic flow taken during quiet breathing. The pre-ejection period (PEP) was measured from the beginning of QRS complex time to the beginning of aortic flow. The left ventricular ejection time (LVET) was measured from the duration of aortic flow. The ratio of the two measurements (PEP/LVET) is the STI index.

M-MODE PARAMETERS OF HEMODIALYSIS PATIENTS:

Table-3 Systolic function

Pre Ejection Period (PEP)
Left ventricular ejection time (LVET)
Systolic time interval index (the ratio of the PEP/LVET)

Table -4 Diastolic function

Isovolumetric relaxation time (IVRT)
‘E’ wave (mitral early filling)
Peak velocity (PV)
‘A’ wave (mitral late filling)
E/A ratio
Deceleration time (DS)

Table-5 Criteria of working group

Systolic dysfunction	STI index > 0.04
Diastolic dysfunction	IVRT > 100 msec or E/A ratio < 1.0 and Deceleration time > 220 msec

STATISTICAL ANALYSIS

The statistical analysis was carried out with the use of a statistical package for social sciences (SPSS) for window ver5.0 Numerical variables were given as mean±SD. Non-numerical parameters were given as frequency and percentage. Group analysis was performed with the use of an unpaired students t-test. 'P' values < 0.05 were accepted as significant.

RESULTS

Left ventricular hypertrophy was present in 40% of the hemodialysis patients. Left ventricular wall thickness, left ventricular diastolic and systolic internal diameters, aortic root, left atrial dimensions and left ventricular mass index were increased in hemodialysis patients compared with controls. There was no difference in the left ventricular ejection fraction (EF 74.08 Vs 73.72% P= not significant) and fractional shortening (FS 34.92 Vs 35.64%, P= not significant) between hemodialysis patients and controls.

In assessment of systolic time intervals, both pre- ejection period (PEP) and systolic time interval index (STI index) were significantly higher in hemodialysis patients compared with controls.

(PEP 69.20m sec Vs 69.20 m sec P= 0.000) (STI index 0.3252 Vs 0.2716 P=0.000). The difference in left ventricular ejection time between hemodialysis patients and controls is not statistically significant (LVET 217.60 m sec Vs 231.84 m sec P= 0.224).

Prolonged STI index (>0.4) was present in 40% of hemodialysis patients.

In our controlled study, 44% of hemodialysis patients had hypertension and left ventricular hypertrophy. Hemodialysis patients were compared according to the presence or absence of hypertension, to assess whether the differences observed in STI parameters will be sustained across these subgroups. The PEP and STI indexes were similar between patients with or without Hypertension. The STI index (0.3579 in normotensive group Vs 0.2716 in control group P= 0.045 statistically significant) is still higher in the normotensive hemodialysis group compared with controls suggests the prolonged systolic parameters are independent of the presence of hypertension or left ventricular hypertrophy.

In the assessment of the diastolic function the isovolumetric relaxation time (IVRT) was prolonged >100 msec in six patients 92.4%), deceleration time >220 m sec in eleven patients (44%) and an E/A ratio of less than one in two patients (8%). Two among the 11 patients with prolonged deceleration time also had prolonged

IVRT >100 m sec and E/A ratio less than one. Overall 48% of patients had diastolic dysfunction.

When hemodialysis patients without hypertension were compared with controls, the IVRT was still significantly prolonged. However, the E/A ratio change did not reach statistical significance.

Table -6 Comparison of M Mode Parameters of Hemodialysis Patients to controls

Parameters	***HD Patients***	***Controls***	***P value***
LVEDD mm	50.80	41.92	0.001
IVS mm	11.12	8.04	0.000
LVPW mm	10.80	7.80	0.000
ARD mm	27.60	23.04	0.000
LAD mm	33.92	23.56	0.000
EF%	74.08	73.72	NS
FS%	34.92	35.64	NS

Table -7 Comparison of Doppler parameters between HD patients and controls

Parameters	***HD Patients***	***Controls***	***P value***
PEP msec	69.20	69.20	0.000
LVET msec	217.60	231.84	0.224
STI index	0.3252	0.2716	0.000
E/A ratio	1.630	1.400	0.000
Deceleration Slope msec	194.00	180.00	0.000
IVRT msec	84.80	72.28	0.000
A wave PV msec	0.682	0.624	0.000

Table -8 Subgroup Analysis

Parameters	***Normotensive HD patients***	***Hypertensive HD patients***	***P value***
LVEDD	51.43	50.00	0.536
IVS	1093	11.36	0.601
LVPW	10.64	11.00	0.664
ARD	27.21	28.08	0.607
LAD	33.21	34.82	0.427
EF	72.86	75.64	0.155
FS	34.521	35.445	0.155
PEP	72.86	64.55	0.148
LVET	210.00	227.27	0.545
STI	0.3579	0.2836	0.045
E/A ratio	1.679	1.569	0.601
DS	202.86	182.73	0.333
IVRT	85.71	83.64	0.739
‘E’ wave	1.106	1.003	0.242
‘A’ wave	0.647	0.728	0.454

The most common features of uremic cardiomyopathy namely left ventricular hypertrophy, diastolic dysfunction and systolic dysfunction were present in 40%, 24%, and 40% of our hemodialysis patients respectively. The diastolic dysfunction and latent systolic dysfunction (STI>0.4) were randomly distributed. 90% of patients with systolic dysfunction had normal IVRT. Impaired STI index and prolonged IVRT are independent of the presence of hypertension or left ventricular hypertrophy. 90% of patients with systolic dysfunction had normal IVRT. 84.4% of patients with diastolic dysfunction (IVRT >100 m sec) had normal STI index. Combined systolic and diastolic dysfunctions were present in 12% of our hemodialysis patients. IVRT is more sensitive than E/A ratio in the diagnosis of diastolic dysfunction in our hemodialysis patients.

REVIEW OF LITERATURE

Systolic time interval parameters are useful indexes for the assessment of myocardial systolic function. Deterioration of STI parameters was previously reported in hemodialysis patients[20]. It was also reported that STI index (PEP/LVET) increased after hemodialysis, mainly by the decrease in LVET caused by volume changes. Therefore, the patients were examined the day after hemodialysis in order to exclude the effect of hypervolemia. Left ventricular ejection times of hemodialysis patients were similar to controls, suggesting that all the patients in our study were euvolemic.

In our study, we have observed that in patients on hemodialysis latent systolic and diastolic dysfunction may coexist or be present alone and can be diagnosed using non-invasive Doppler study even before overt decline in the left ventricular ejection fraction.

In a controlled study,[14] echocardiographic findings in 86 hemodialysis patients and 51 healthy controls were compared for STI parameters (PEP, LVET, STI index) and diastolic dysfunction

(IVRT, E/A ratio, and deceleration time). The pre-ejection period (114±21 Vs. 94±4 msec, P <0.001) and STI index (0.41±0.11 Vs. 0.34±0.02 (P<0.001) were higher in hemodialysis patients compared with controls. Increased STI index and prolonged PEP in hemodialysis patients were independent of hypertension and LV hypertrophy. Diastolic dysfunction was present in 61% of patients. The IVRT were also found to be longer in hemodialysis patients compared with controls (97±16 Vs. 75±16 sec P<0.001) independent of the presence of hypertension or LV hypertrophy. In this study 48% of patients with diastolic dysfunction having an STI index within normal limits and the other half of the patients with systolic dysfunction having a normal IVRT. The combined systolic and diastolic dysfunction was observed in 30% of the patients. These authors concluded that systolic and or diastolic dysfunction of the myocardium may appear singly or simultaneously and deterioration of STI indexes can occur before an overt systolic dysfunction (with normal ejection fraction).

In an another study[15] the effects of hemodialysis on left ventricular function were studied with the use of externally recorded LV systolic time intervals and echocardiography. In this

study, ten patients with normal or near-normal predialysis LV function and no circulatory congestion were studied. Hemodialysis significantly decreased LV ejection time (LVET) from 270± 9 msec to 237±10 msec (P=0.001). No significant change was noted in the pre-ejection period (PEP). The STI index (PEP/LVET ratio) increased from 0.41±0.05 to 0.45±0.06 (P=<0.05). Hemodialysis was also associated with a 17% decrease in LV stroke volume. Ejection fraction and fractional shortening did not change significantly. Small changes in heart rate and blood pressure were insignificant. The authors concluded that post dialysis reduction in stroke volume was due primarily to an acute decrease in LV preload and dialysis also appears to be associated with a small increase in LV contractile state.

STI offer temporal description[7] of the sequential phases of cardiac cycle which are influenced physiologically by the same variables which affect other measures of LV performance. The STI offer a measure of LV function because of extreme sensitivity of this variable and ease of its measurement, the STI are well suited for studying the effect of pharmacologic agents on heart[7].

In a study of 11 patients[16] with chronic kidney disease and hypertension, the responses in the left ventricular systolic time intervals following Digoxin administration (0.5 mg intravenously) were studied. The control group comprised 11 patients with mild essential hypertension. There were no clinical signs of congestive heart failure in any of the patients. Authors reported that uremic patients had longer pre-ejection period and higher STI index compared with controls. Digoxin administration induced a reduction in PEP and STI index. These data suggest the presence of latent left ventricular systolic dysfunction in the patients with chronic kidney disease that improved after administration of digoxin.

Parfrey PS[6] studied the outcome and risk factors for LV disorders (concentric LVH, LV dilatation with or without LV hypertrophy, Systolic dysfunction) in patients with chronic uremia. A cohort of 432 ESRD patients who survived at least 6 months had an echocardiogram on initiation of dialysis therapy and subsequently clinical, laboratory, echocardiography data was obtained annually. On initiation of ESRD therapy, 16% of patients had systolic dysfunction, 41% concentric LVH, 28% LV dilatation,

and only 16% had normal echocardiogram. Median time to development of heart failure was 19 months in patients with systolic dysfunction, 38 months in patients with concentric LVH and LV dilatation.

The relative risks of heart failure in the three groups were significantly worse than in the normal group after adjusting for age, diabetes, and ischemic heart disease. Median survival was 38 months in patients with systolic dysfunction, 48 months in concentric LVH, 56 months in LV dilatation and 66 months in the normal group. Follow up echocardiography revealed the degree of concentric LVH was independently related to hypertension, old age, anemia while on dialysis. The degree of LV dilatation was related to anemia, IHD, hypertension and hypoalbuminemia while on dialysis. The degree of systolic dysfunction was associated with anemia and IHD. Authors concluded that manifestations of LV disease are frequent in chronic uremia and are associated with high risks of heart failure and death. Potentially reversible factors include anemia, hypertension, hypoalbuminemia and ischemic heart disease.

Pre-ejection period consists of two components. The electrical component, which begins with the ‘Q’ wave in ECG and represents the dispersion of the electrical wave front from endocardium to epicardium, and a mechanical contraction component that continues until the aortic valve opens. In uremia, both electrical and mechanical components of the PEP may be compromised by intermyocardiocytic fibrosis caused by an increase in collagen content[17].

In an animal experimental study[18], the relations between hypertrophy, fibrosis, and diastolic performance in early experimental hypertension, 18 control dogs, and 12 dogs with experimental left ventricular hypertrophy were studied. Diastolic function was impaired in dogs with left ventricular hypertrophy as indicated by a decrease in Doppler-derived E/A ratio and prolonged isovolumetric relaxation time (IVRT).

At post mortem examination, the hypertensive left ventricle weighed significantly more than normal and had greater muscle fiber diameter. In contrast, neither percent fibrosis nor fibrotic volume was significantly increased in normal dogs. The conclusion

from this experimental study was, diastolic dysfunction may exist in the setting of hypertrophy and increased myocyte size was associated with early diastolic filling abnormalities characteristic of the hypertensive left ventricle.

Abnormal diastolic relaxation is most reliably detected by pulsed Doppler measurement of the velocity of the ‘E’ (early, passive) and ‘A’ (atrial, active) components of diastolic flow across the mitral valve. Decreased left ventricular compliance caused by impaired relaxation results in decreased E/A ratio and is frequently seen in patients with chronic kidney disease as a result of left ventricular hypertrophy. Diastolic dysfunction is associated with an increased risk of intradialytic hypotension, as relatively small reductions in left atrial filling have marked effects on cardiac output.

Interstitial myocardial fibrosis, a prominent finding in uremia had been shown to be more marked in hemodialysis patients compared with patients who have diabetes mellitus or essential hypertension with similar LV mass[24].

A recent experimental and clinical study[23] suggest (a) that cardiac hypertrophy can be dissociated from hypertension and that blood pressures may have only a permissive role, (b) that experimental uraemia is associated with specific activation of pericytes and intermyocardiocytic fibrosis. Cardiac hypertrophy not correlated with elevated blood pressure, and intermyocardiocytic fibrosis not observed in similarly hypertensive non-uraemic patients, have recently been documented in dialysis patients. The implications of these findings may be (a) electrical instability and predisposition to a sudden cardiac death and (b) diastolic cardiac malfunction with impaired LV filling and predisposition to dialysis hypotension. Some evidence for the latter possibility is provided.

A paper updates[9] the current view on clinical significance of systolic time intervals (STI) in estimating the cardiac changes associated with hypertension. The following three intervals were measured as STI: (1) electromechanical systole (QS2 interval); (2) left ventricular ejection time (LVET) and (3) pre-ejection period (PEP). Firstly, the influences of changes in heart rate, preload, after load and myocardial contractility upon each interval were reviewed;

secondly, clinical applications of STI in various types of hypertension such as essential hypertension, hypertension with angina pectoris and pheochromocytoma were studied. In patients with essential hypertension, there was a good positive correlation between PEP and left ventricular mass, and a shortening of LVET was observed only at the decompensated stage. The changes in STI in angina pectoris with or without hypertension were similar and were different from those in essential hypertensives. STI in patients with pheochromocytoma were characterized by a marked shortening of QS2 and LVET with normal PEP. These findings indicate the usefulness of STI in detecting cardiac changes in various types of hypertension.

An investigation[12] was performed to determine whether variables obtained directly from the Doppler left ventricular diastolic flow velocity profile provide a reliable estimate of diastolic function. Measurements of diastolic flow velocity obtained by Doppler echocardiography were compared with volumetric measurements of left ventricular diastolic filling determined by radionuclide angiography in 12 subjects without cardiac disease and in 25 patients with a variety of cardiac diseases. The two methods

were in agreement in distinguishing normal from abnormal diastolic function in 21(84%) of the 25 patients with cardiac disease, identifying diastolic function as normal in 8 and abnormal in 13 of these patients. Good correlations were observed between certain Doppler variables of left ventricular diastolic flow velocity and radionuclide angiographic variables of left ventricular filling. The time interval from the aortic closing component of the second heart sound to the end of the early diastolic flow velocity peak, assessed with Doppler echocardiography, correlated well with the time interval from end-systole to the end of rapid filling, assessed with radionuclide angiography ($r = 0.83$). Descent of the Doppler early diastolic flow velocity peak correlated well with the radionuclide angiographic peak filling rate ($r = 0.79$). The ratio between the heights of the early and late (due to atrial systole) peaks of diastolic flow velocity showed good correlation with the ratio between percent of left ventricular filling during rapid filling and during atrial systole (r 0.76). These findings demonstrate that the left ventricular diastolic flow velocity profile obtained with Doppler echocardiography compares favorably with radionuclide

angiographic variables in the evaluation of left ventricular diastolic function.

London et al[19] studied cardiac hypertrophy and arterial alterations in end-stage renal disease. He observed Left ventricular (LV) hypertrophy is the most common cardiovascular alteration in end-stage renal disease patients. LV hypertrophy results from chronic flow and pressure overload and combine features of concentric and eccentric hypertrophy. The causes of chronic flow overload are the presence of AV shunt, salt and water overload, and anemia. The pressure overload is related to alterations of physical properties of large arteries characterized by an increased arterial and aortic stiffness. The systolic function of hypertrophied ventricle is preserved, but the diastolic filling is impaired. The ventricular hypertrophy progresses over the time on hemodialysis together with a progressive worsening of both systolic and diastolic functions.

Foley RN[20] studied clinical and echocardiographic disease in patients starting end-stage renal disease therapy. In this study a prospective cohort of 433 ESRD patients was followed from the start of ESRD therapy for a mean of4l months. Baseline clinical

assessment and echocardiography were performed on all patients. The major outcome measure was death while on dialysis therapy. Clinical manifestations of cardiovascular disease were highly prevalent at the start of ESRD therapy: 14% had coronary artery disease, 19% angina pectoris, 31% cardiac failure, 7% dysrhythmia and 8% peripheral vascular disease. On echocardiography 15% had systolic dysfunction, 32% left ventricular dilatation and 74% left ventricular hypertrophy. The overall median survival time was 50 months. Age, diabetes mellitus, cardiac failure, peripheral vascular disease and systolic dysfunction independently predicted death in all time frames. Coronary artery disease was associated with a worse prognosis in patients with cardiac failure at baseline. High left ventricular cavity volume and mass index were independently associated with death after two years. The independent associations of the different echocardiographic abnormalities were: systolic dysfunction, older age and coronary artery disease; left ventricular dilatation-male gender, anemia, hypocalcemia and hyperphosphatemia; left ventricular hypertrophy, older age, female gender, wide arterial pulse pressure, low blood urea and hypoalbuminemia. Authors conclude that clinical and

echocardiographic cardiovascular disease are already present in a very high proportion of patients starting ESRD therapy and are independent mortality factors.

A cross sectional study[21] was done to see whether cardiac morphological and functional abnormalities in uraemic patients are determined by high blood pressure or if they are an expression of a specific cardiomyopathy in a City general hospital in Italy. In this study 35 uraemic patients receiving haemodialysis (17 men, 18 women; mean age 60.3 (11.2); mean duration of dialysis 52 months) were selected from the 64 patients in Venice who were receiving dialysis; subjects with diabetes, haemochromatosis, valvar dysfunction, regional dyskinesias, and pericarditis were excluded. 19 control normotensive subjects (6 men and 13 women), matched for age. Main outcome measures was echocardiographic measurements of left atrium, left ventricular end diastolic and end systolic volume, aortic root diameter, posterior wall and interventricular septum thickness, left ventricle mass index, and ejection fraction in controls and in patients according to whether they were normotensive (five men, eight women) or hypertensive (12 men, 10 women) on 48 hour ambulatory monitoring; left

ventricular diastolic function by Doppler ultrasonography. The results of the study was mean systolic and diastolic pressures, daytime systolic and diastolic pressures, and night time systolic and diastolic pressures were significantly higher in the hypertensive patients than in the normotensive patients. The normotensive patients had similar blood pressures to the controls. Left ventricular mass correlated significantly with the mean diastolic pressure and mean night time systolic and diastolic pressures. Parathyroid hormone concentrations were similar in the two groups of patients. Diastolic relaxation was impaired to the same degree in the two groups of patients. Parameters of diastolic function showed no relation to left ventricular mass, which was significantly higher in the hypertensive than in the normotensive patients. Authors concluded uraemia is likely to induce specific changes in the relaxation properties of the myocardium. These changes are responsible for the impaired diastolic function independently of blood pressure, degree of hypertrophy, and metabolic changes, which suggests the existence of a specific cardiomyopathy. Hypertension remains a determinant of left ventricular mass.

The acute effects of hemodialysis on left ventricular (LV) function were studied[15] with the use of externally recorded LV systolic time intervals and echocardiography; 10 patients with normal or near-normal predialysis LV function and no circulatory congestion were studied. Hemodialysis significantly decreased the LV ejection time (LVET) from 270 ± 9 ms to 237±10 ms (p=< 0.001); no significant change was noted in the pre-ejection period (PEP). The PEP/LVET ratio increased from 0.41±0.05 to 0.45±0.06 (p =<0.05). The LV end-diastolic dimension decreased from 5.3± 0.3 cm to 4.8± 0.3 cm (p=<0.001). Fractional shortening and ejection fraction did not change significantly, but hemodialysis slightly increased mean VCF from 1.2 ± 0.1 s-1 to 1.4± 0.1 s-1 (p =<0.005). Hemodialysis was associated with a 17% decrease (87±8 ml to 72±7 ml; =<than 0.001) in LV stroke volume as calculated from echocardiographic data. Small changes in heart rate and blood pressure were insignificant. The conclusion of this study was that the postdialysis reduction in stroke volume was due primarily to an acute decrease in LV preload; dialysis also appears to be associated with a small increase in the LV contractile state.

In an autopsy study[17], Heart was examined in 31 patients with uremia not on dialysis, 42 patients on hemodialysis for less than six months, 60 patients on hemodialysis for more than six months. 16 patients after renal transplantation and 11 patients on CAPD. Patients with stenosing coronary artery lesions were excluded. Diffuse non-coronary intermyocardiocytic fibrosis, assessed by a score system in trichrome - stained sections, was found in 91% of chronically uremic patients but not in non-hypertensive, non diabetic controls. The lesion was present even in non-dialysed uremic patients. In dialysed patients, its severity was related to the duration of dialysis and it was demonstrable even years after renal transplantation. Authors concluded that uremia is an important determinant of intermyocardiocytic fibrosis independent of hypertension, diabetes, anemia,heart weight and presence or absence of dialysis procedure.

DISCUSSION

Uremic patients may present with

- Left ventricular hypertrophy
- Congestive heart failure/ Hypervolemia
- Ischemic heart disease
- Acquired valvular heart disease
- Arrhythmias

RISK FACTORS:

Cardiovascular causes of death are most prominent in the first few years of dialysis and are rare in patients who have been on long-term dialysis. Risk factors for cardiovascular disease in patients on dialysis are

- Dyslipidemia
  - hypercholesterolemia
  - hypertriglyceridemia
  - decreased HDL

  - increased VLDL increased
  - lipid peroxidation

- Hyperinsulinemia
- Hypercoagulability
- Hypertension
- Smoking
- Obesity
- Sedentary life style

Other causes specific to uremia:

- Hyperparathyroidism
- Phosphate retention
- Iatrogenic iron overload
- Inadequate dialysis
- Hyperhomocystinemia (folate, pyridoxine deficiency)
- Endothelial dysfunction
  - increased Endothelin

  - impaired nitric oxide production,
  - hyperhomocystinemia,
  - increased oxidative stress

- Carbamylation of matrix proteins
- Decreased anti-oxidant defence.

Is there a specific uremic cardiomyopathy?

It has been proposed that uremia per se leads to impaired myocardial contractile function. Improvement after institution of dialysis or after successful transplantation suggests a dialyzable uremic toxin rather than structural alterations or ischemic damage, although chronic volume overload may be responsible by causing a reversible dilated cardiomyopathy. Improvement in contractile function acutely during hemodialysis suggesting that a dialyzable uremic toxin has a direct and readily reversible cardiodepressant action.

In the past, cardiac changes in renal failure have commonly been ascribed to hypertension and poorly specified toxic effects of uremia. In a study by Ritz E et al[5] demonstrated that cardiac

hypertrophy can be dissociated from hypertension and that blood pressure may have only a permissive role and experimental uremia is associated with specific activation of pericytes and intermyocardiocytic fibrosis.

In the recent HEMO study, the most common cause of death in dialysed patients was ischemic heart disease (20.4%) followed by cardiac rhythm disorder (10.4%), cerebrovascular disease (8.6%) and infections (7.7%)[16]. The prospective Canadian study reported an incidence of approximately 10% per year for both ischemic heart disease and cardiac failure significantly higher than the values seen in the general population. The features of uremic cardiomyopathy like Left ventricular hypertrophy, diastolic dysfunction and systolic dysfunction were detected in 40%, 24% and 40% of our hemodialysis patients. These rates were comparable to those reported in previous studies[17-19].

LEFT VENTRICULAR HYPERTROPHY:

In non-renal patients, hypertension and left ventricular hypertrophy are closely related, but this relationship is less marked in patients with renal failure[22]. LV hypertrophy develops in uremic

animals despite normalization of blood pressure by administration of angiotensin converting enzyme inhibitors, alpha and beta blockers or diuretics[18]. LV hypertrophy progresses with time on dialysis even when patients kept normotensive[15]. In the study of Parfrey[6], 71% of non-diabetic dialysis patients without dilated cardiomyopathy had LV hypertrophy and in majority of patients this progressed over a period of 3-4 years.

LV hypertrophy is more frequent in early stages of CKD and increases progressively. So that it is found in approximately 70% of patients starting renal replacement therapy. Initially concentric LVH is seen, while in later stages more frequently eccentric LVH prevails. LVH tend to be associated with hypertension, anemia, high arteriovenous fistula flow and poor control of volume overload. At an early stage systolic function is usually normal or even increased but evidence of diastolic dysfunction can be found even in asymptomatic patients. LVH is not an innocent finding, it is an independent predictor of death in dialysis patients.

Congestive Heart Failure:

Ten percent of non-diabetic dialysis patients were found to have congestive heart failure[15]. Nonspecific ancillary findings in patients with congestive heart failure are a history of dyspnea, edema, cardiomegaly, raised JVP, basal crepitations, pulmonary venous hypertension or interstitial edema on chest radiography.

The most common cause of congestive heart failure in CKD patients is ischemic heart disease, but the other factors are

Hemodynamic factors:

- Hypertension
- Hypervolemia
- Renal Anemia
- Arteriovenous fistula
- Acquired valvular heart disease
- Pericarditis

Non-hemodynamic factors:

- Ischemic heart disease
- Cardiomyopathy

- Autonomic dysfunction
- Excess PTH
- Aluminium overload
- Iron overload
- Myocardial calcification
- Metabolic acidosis
- β_2 microglobulin amyloidosis

NON-MODIFIABLE RISK FACTORS:

Age:

As with ischemic heart disease, age is an important clinical marker of risk for left ventricular hypertrophy in the general population, chronic renal disease patients and hemodialysis population.

Sex:

The role of sex as a risk factor for left ventricular hypertrophy and systolic dysfunction is less clear. In a registry-based study[24]

women were found to be more likely to have radiographic cardiomegaly or history of congestive heart failure and less likely to have ECG or echocardiographic evidence of LVH than men. Moreover, female sex was associated with concentric LVH whereas male sex was associated with LV dilatation and congestive heart failure.

MODIFIABLE RISK FACTORS:

Hypertension:

Hypertension is associated with increased risk of chronic kidney disease progression and earlier onset of dialysis. A lower than usual target blood pressure (<125/75 mmHg) appears more effective in delaying renal decline than usual goal (<140/90) in patients with proteinuria more than 1g/day. In patients on dialysis, each 10 mm Hg increment in blood pressure is associated with a 48% higher risk for development of LVH[25].

Anemia:

Anemia is associated with LV dilatation and LVH in CKD and dialysis patients the relative risk for LVH progression per 10 g/L drop is 1.74 in CKD and 1.48 in dialysis patients[26]. Anemia also is a

risk factor for the development of cardiac failure and death in dialysis patients. Normalisation of haemoglobin prevent progressive LV dilatation in those with normal cardiac volumes at baseline but not in patients with established cardiac disease[27-28].

Ischemic heart disease:

IHD is an important cause of systolic and diastolic dysfunction in the general population and in patients on dialysis[29]. CAD may exacerbate ischemia, myocyte attrition and cardiac interstitial fibrosis. Myocyte apoptosis, ischemia, and neurohormonal activation are thought to contribute myocardial dysfunction.

Hypoalbuminemia:

Several studies have shown that hypoalbuminemia is a powerful predictor of poor outcome in patients with ESRD. Hypoalbuminemia is associated with LV dilatation and predisposes to cardiac failure[30]. The mechanism underlying this association are unknown. Hypoalbuminemia is associated with a hypercoagulable state and therefore may predispose to myocardial infarction and ischemic cardiomyopathy.

Hypervolemia:

Salt and water retention is a persistent problem in patients on dialysis and is less problematic in early stages of CKD. Blood volume correlates directly with LV diameter in patients on hemodialysis[31] as does the magnitude of interdialytic weight gains. LV diameter decreases with volume contraction during hemodialysis. By definition, salt and water overload is blood volume overload and hence plays a causal role in the development of LVH. Keeping the patient's dry weight optimal can minimise the degree of enlargement of the LV[5].

In chronic hemodialysis patients, two groups were identified with regard to congestive heart failure. One without a previous history of congestive heart failure and the other with a history of congestive heart failure at initiation. The independent predictors of congestive heart failure at initiation of hemodialysis are age, diabetes, ischemic heart disease, systolic dysfunction on baseline echocardiogram. In patients free of baseline congestive heart failure the predictors of CHF are hypertension, anemia, hypoalbuminemia and hypocalcemia. Factors that predispose to volume or flow overload (Anemia), pressure overload (Hypertension) and cell

death (malnutrition, hyperparathyroidism, hypocalcemia, ischemic heart disease) are associated with congestive heart failure in dialysis.

Congestive heart failure may result from systolic dysfunction or diastolic dysfunction, the latter occurring because of left ventricular concentric or eccentric hypertrophy. Ischemic heart disease is an additional independent predictor. Among patients with diastolic dysfunction, congestive heart failure results from impaired ventricular relaxation. This leads to an exaggerated increase in left ventricular end-diastolic pressure for a given increase in end diastolic volume. As a result, small excess of salt and water can rapidly lead to large increase in left ventricular end-diastolic pressure, culminating in pulmonary edema. In dilated cardiomyopathy, cardiac output is maintained at the expense of an increase in both end-diastolic fibre length and end-diastolic volume. As ventricular volume increases, failure to achieve adequate hypertrophy leads to an increase in wall stress and increase in end-diastolic pressure, leading ultimately to pulmonary edema.

Structural changes in the heart, LVH, cardiac fibrosis and myocardial calcification have major impact on cardiac function. LVH and cardiac fibrosis are associated with impaired LV compliance. This explains why patients with CKD develop heart failure so easily when atrial fibrillation supervenes. Reduced LV compliance also increases the risk of pulmonary edema during hypervolemia because the increase in LV volume during hypervolemia cause a more marked rise in LV and diastolic volume and pressure which lead to poor tolerance of hypervolemia. Congestive heart failure carries a poor prognosis. Acturial survival at 2 years is not more than 33% as compared to 80% in patients without heart failure[15].

Previous studies[14] reported 61% diastolic dysfunction in 61% of 86 patients, with nearly 48% of patients with diastolic dysfunction having an STI index within normal limits and the remaining 52% of patients with systolic dysfunction having a normal IVRT. In comparison with this study, we observed, 24% of our patients had diastolic dysfunction and 40% had systolic dysfunction. These rates were definitely less than to those reported in the previous study[14]. This may be related to the small sample size

of our study. We also observed combined systolic and diastolic dysfunction in only 12% of our patients which is again very low compared to the previous study in which 30% of patients had combined systolic and diastolic dysfunction.

Our study markedly differs from the previous one where only half of the patients with systolic or diastolic dysfunction had normal IVRT or STI index. But in our study, 90% of patients with systolic dysfunction had normal IVRT and 84.4% of patients with diastolic dysfunction had normal STI index. However, as in the previous study, the impaired STI index, and prolonged IVRT are independent of the presence of hypertension or left ventricular hypertrophy and IVRT is more sensitive than E/A ratio to diagnose diastolic dysfunction.

In our study, we have observed that in hemodialysis patients, latent systolic or diastolic dysfunction may coexist or be present alone, and can be diagnosed using non-invasive Doppler study even before overt decline in the left ventricular ejection fraction.

CONCLUSION

1. The most common features of uremic cardiomyopathy namely left ventricular hypertrophy, diastolic dysfunction and systolic dysfunction were present in 40%, 24%, and 40% of our hemodialysis patients respectively.

2. The diastolic dysfunction and latent systolic dysfunction (STI>0.4) were randomly distributed.

3. Impaired STI index and prolonged Isovolumetric relaxation time are independent of the presence of hypertension or left ventricular hypertrophy.

4. 90% of patients with systolic dysfunction had normal Isovolumetric relaxation time.

5. 84.4% of patients with diastolic dysfunction (IVRT >100 m sec) had normal STI index.

6. Combined systolic and diastolic dysfunction were present in 12% of our hemodialysis patients.

7. Isovolumetric relaxation time is more sensitive than E/A ratio in the diagnosis of diastolic dysfunction in our hemodialysis patients.

LIMITATIONS OF OUR STUDY

- Small sample size.
- No follow up echocardiogram to assess the increased risk of developing heart failure in future.
- Potential reversible factors like anemia, hypoalbuminemia and its effects on latent systolic dysfunction are not defined.

MASTER CHART

CRF PATIENTS ON HEMODIALYSIS

S.No	Age	Sex	Predialytic urea Mg/dl	Predialytic scr Mg/dl	URR %	Hb g/dl	S.Alb g/dl	LVEDD mm	IVS mm	LVPW mm	ARD mm	LAD mm	EF%	FS%	PEP M.sec	IVET	STI	E/A ratio	DS M.sec	IVRT M.Sec	E wave PV	A wave PV	NKD	HT/LVH
1	19	M	189	9.6	47	8.3	5.4	48	13	12	23	35	77	38.8	60	210	0.28	2.4	130	60	1.2	0.5	CGN	+
2	35	M	87	8.5	54	8.8	4	57	13	13	29	40	68	31	40	200	0.2	1.56	220	90			CGN	+
3	19	M	135	8.2	74	8.2	5.6	51	11	11	25	40	75	36.8	50	270	0.14	2.5	130	70	1.4	0.56	CGN	+
4	45	M	145	7.6	68	10.6	5.6	49	12	12	34	38	78	39.6	50	210	0.2	0.96	240	80	0.96	1	CGN	+
5	23	M	165	8.5	69	8.8	5.5	52	13	13	30	36	80	41.4	50	200	0.25	1	120	70	1.3	1.19	CGN	+
6	40	M	157	10.2	66	8.6	4.2	53	8	8	34	34	78	39.8	70	280	0.25	1.4	220	100	1.01	0.71	CGN	+
7	37	M	123	9.3	67	8	3.9	52	12	11	27	34	67	28	80	200	0.4	2.02	130	80	0.87	0.43	CGN	+
8	27	M	153	7.9	69	8	3.5	47	10	10	28	24	67	30	80	340	0.23	1.49	170	90	1	0.67	CGN	+
9	34	M	91	6.7	61	9	3.4	39	10	10	23	27	80	35.5	80	190	0.42	1.2	200	80	0.5	0.4	CGN	+
10	32	M	165	9.2	70	7.8	3.7	45	13	12	28	38	82	43	80	180	0.44	2.1	170	80	0.9	0.42	CGN	+
11	26	F	73	6.8	60	8.8	3.5	59	11	11	37	37	66	30	70	20	0.31	1.2	240	100			CGN	-
12	34	F	72	5.3	52	8.8	3.8	52	12	12	25	35	78	39	80	340	0.23	1.9	220	90	1.15	0.58	CGN	-
13	19	F	60	7.2	58	8	4	42	7	7	25	29	78	38	70	250	0.28	1.4	270	70	1.3	0.9	CGN	-
14	18	F	111	5.6	63	8	3.5	43	7	7	20	25	75	37	80	180	0.44	1.4	160	60	1.2	0.83	CGN	-
15	27	F	117	6.9	65	8.8	3.3	42	8	8	20	25	77	38	80	190	0.42	2.1	170	70	1.2	0.55	VUR	-
16	32	M	90	7.7	66	8.5	4	57	10	9	28	37	80	26	70	220	0.31	0.63	280	120	0.89	1.4	CIN PUV	+
17	33	M	105	9.5	61	8	4.2	53	12	10	31	28	70	33	40	260	0.34	1.3	130	80	0.78	0.58	CIN	-
18	33	M	147	8.5	65	10	4.5	58	12	12	26	39	70	30	70	160	0.43	2.1	150	70	1.2	0.57	CIN	-
19	33	M	153	9	61	9	3.5	55	9	8	28	35	74	35.7	60	160	0.43	1.4	240	90	1.2	0.82	CIN	-
20	28	M	120	6.8	65	9.2	4	58	12	12	30	40	70	30	70	280	0.25	1.6	230	110	0.92	0.57	CIN	-
21	17	M	123	9	59	10.5	4.8	52	12	12	29	37	69	32	70	160	0.43	2.5	130	100	1.29	0.5	CIN	-
22	31	M	147	10.1	65	9.4	3.3	48	13	13	30	33	75	38	90	320	0.28	2.3	190	90	1.1	0.46	CIN	-
23	29	M	123	6.9	59	9.5	3.8	48	14	14	26	33	75	36.8	90	260	0.34	1.4	260	100	0.92	0.62	CIN	-
24	23	M	92	6.4	67	8.8	3.5	55	13	12	24	35	69	29.8	80	200	0.4	1.4	250	90	1.09	0.76	CIN	-
25	26	M	157	8.5	70	8.4	3.3	55	11	11	30	34	74	36	70	160	0.43	1.5	200	80	1.03	0.67	CIN	-

HEALTHY CONTROLS

S.No	*Age*	*Sex*	*Urea mg/dl*	*Scr mg/dl*	*Hb (g/dl)*	*S.Alb (g/dl)*	*LVEDD mm*	*IVS mm*	*LVPW mm*	*ARD mm*	*LAD mm*	*EF %*	*FS %*	*PEP m.Sec*	*IVET*	*STI*	*E/A ratio*	*DS M.sec*	*IVRT M.Sec*	*E wave PV*	*A wave PV*
1	30	F	20	0.6	14	6	42	8	7	23	23	75	35	68	280	0.24	1.4	180	71	1	0.68
2	35	M	25	0.8	15	5.5	38	7	7	22	22	74	34	74	280	0.26	1.6	180	68	0.84	0.52
3	27	M	25	0.8	16	6	45	9	8	24	25	72	38	70	230	0.3	1.5	180	78	0.94	0.62
4	25	F	20	0.7	13.5	5.3	40	7	8	24	25	75	35	69	240	0.27	1.3	180	68	0.8	0.6
5	28	F	26	0.8	14	5.5	42	8	7	22	22	70	34	65	230	0.28	1.2	180	78	0.9	0.7
6	30	M	26	0.8	16	6	43	9	7	23	23	82	38	68	28	0.24	1.2	180	71	0.9	0.7
7	37	M	25	1	15	5.4	44	8	8	22	25	70	35	74	280	0.26	1.3	180	71	0.8	0.6
8	35	F	26	0.9	13	5.5	40	7	8	23	23	75	34	70	230	0.3	1.4	180	68	1	0.68
9	40	F	24	0.9	12.5	5.3	45	9	7	24	24	76	38	69	240	0.28	1.5	180	78	0.94	0.62
10	42	M	26	0.8	13	5.8	39	8	8	22	25	70	35	65	230	0.28	1.5	180	71	0.94	0.62
11	32	M	24	0.6	15	6	38	7	7	23	23	75	34	65	230	0.28	1.4	180	68	1	0.68
12	33	M	25	0.7	14	5.6	40	9	8	24	24	70	38	69	240	0.28	1.3	180	78	0.8	0.6
13	35	M	26	0.8	13	5.3	42	9	8	24	25	80	35	70	230	0.3	1.2	180	71	0.9	0.7
14	40	M	25	0.9	14	5.5	43	7	8	23	23	75	34	74	280	0.26	1.6	180	68	0.84	0.52
15	38	M	24	1	15	5.8	44	8	7	22	24	70	38	68	28	0.24	1.6	180	71	0.84	0.52
16	40	M	26	1	13	5.8	45	8	7	22	23	72	38	65	230	0.28	1.5	180	78	0.94	0.62
17	41	M	25	0.9	13.5	5.5	39	7	8	23	22	74	35	69	240	0.28	1.4	180	68	1	0.68
18	45	M	26	0.8	12.5	5.3	40	9	7	24	24	74	34	70	230	0.3	1.3	180	68	0.8	0.6
19	30	F	24	0.7	13	5.5	38	8	8	22	25	75	34	74	280	0.26	1.2	180	71	0.9	0.7
20	23	F	26	0.6	13	5.3	43	7	7	23	24	70	35	68	280	0.24	1.2	180	78	0.9	0.7
21	30	F	26	0.8	12.5	5.8	44	9	9	24	22	74	38	68	280	0.24	1.3	180	71	0.8	0.6
22	30	F	24	0.7	12.5	5.5	45	9	9	24	22	73	34	74	280	0.26	1.4	180	68	1	0.68
23	35	M	24	0.9	14	6	40	7	9	23	22	72	35	70	230	0.3	1.5	180	78	0.94	0.62
24	37	M	24	1	14	6	44	8	9	22	24	75	35	69	240	0.28	1.6	180	71	0.84	0.52
25	23	F	25	0.8	14	6	45	9	9	24	25	75	38	65	230	0.28	1.6	180	78	0.84	0.52

ABBREVIATIONS

ARD	-	Aortic Root Diameter
AVS	-	Arterio Venous Shunt
CKD	-	Chronic Kidney Disease
CVD	-	Cardiovascular Disease
CAD	-	Coronary Artery Disease
DS	-	Deceleration slope
ECG	-	Electrocardiogram
ECHO	-	Echocardiogram
ESRD	-	End stage renal disease
EF	-	Ejection Fraction
FS	-	Fractional Shortening
HDL	-	High density lipoprotein
IVRT	-	Isovolumetric relaxation time

IVS	-	Interventricular Septum
IHD	-	Ischemic heart disease
LVET	-	Left ventricular ejection time
LVPW	-	Left ventricular posterior wall
LAD	-	Left atrial diameter
LVEDD	-	Left ventricular end diastolic diameter
LVH	-	Left ventricular hypertrophy
PEP	-	Pre ejection period
PTH	-	Parathyroid hormone
SD	-	Standard deviation
STI	-	Systolic Time interval
URR	-	Urea reduction rate

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